STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 173570

TO: Deborah Lambkin **Location: REM-5C09&5C18** **Art Unit: 1626** **December 21, 2005** **Case Serial Number: 10/719465**	**From: P. Sheppard** **Location: Remsen Building** **Phone: (571) 272-2529** **sheppard@uspto.gov**

Search Notes

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L5        27407 SEA SSS FUL L3
L6              STR
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      FILE 'HCAPLUS' ENTERED AT 12:00:59 ON 21 DEC 2005
L8            6 SEA ABB=ON  PLU=ON  L7
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      FILE HCAPLUS

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      FILE LAST UPDATED: 20 Dec 2005  (20051220/ED)

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       This file contains CAS Registry Numbers for easy and accurate
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FILE COVERS 1907 - 21 Dec 2005  VOL 143 ISS 26
FILE LAST UPDATED: 20 Dec 2005  (20051220/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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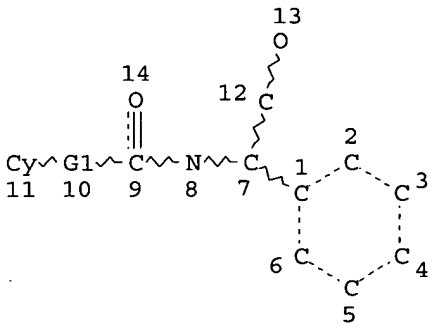


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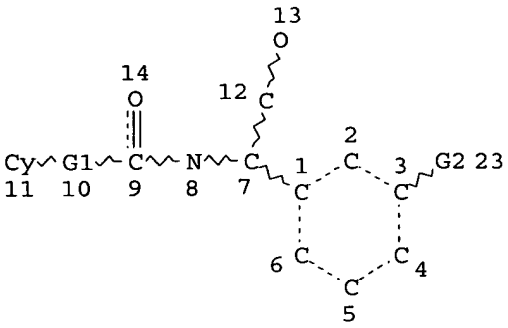

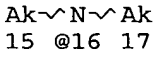

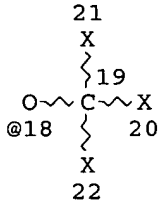

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L8 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:470948 HCAPLUS
DOCUMENT NUMBER: 141:38448
TITLE: Preparation of arylcyclopropylcarboxylic amides as potassium channel openers
INVENTOR(S): Wu, Yong-jin; Sun, Li-qiang; L'heureux, Alexandre
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047738	A2	20040610	WO 2003-US37305	20031121
WO 2004047738	A3	20041007		

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US 2004110754 A1 20040610 US 2003-719184 20031121
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: US 2002-428337P P 20021122
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OTHER SOURCE(S): MARPAT 141:38448

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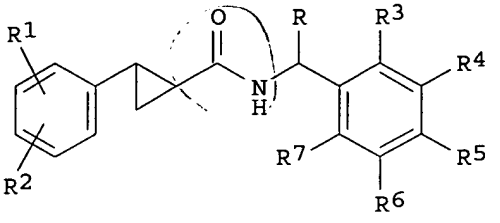

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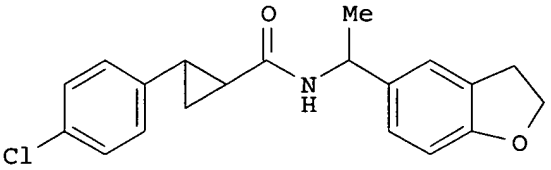


II

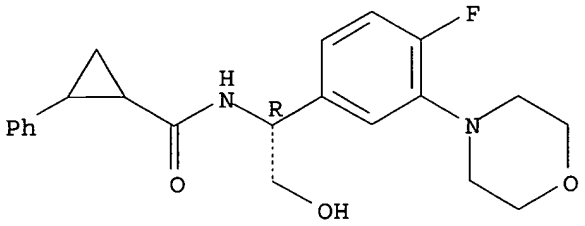
AB The title compds. [I; R = alkyl, CF3, hydroxymethyl; R1, R2 = H, alkyl, halo, morpholin-4-yl; R4 = (un)substituted morpholin-4-yl, pyridinyl, pyrimidinyl, etc.; R5 = H, F; or R4 and R5 taken together = CH:CHCH:CH, CH2CH2O; R3, R6, R7 = H, F] which are openers or activators of KCNQ potassium channels (biol. data given), were prepared Thus, amidation of 1-(2,3-dihydrobenzofuran-5-yl)ethylamine with 2-(4-chlorophenyl)cyclopropanecarboxylic acid afforded the amide II. The present invention also provides pharmaceutical compns. comprising the compds. I, and the method of treatment of disorders sensitive to KCNQ potassium channel opening activity such as migraine or a migraine attack, bipolar disorders, epilepsy, acute and chronic pain and anxiety.

IT **701913-77-1P 701913-78-2P 701913-79-3P**
701913-80-6P 701913-81-7P 701913-82-8P
701913-83-9P 701913-84-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylcyclopropanecarboxamides as potassium channel openers)

RN 701913-77-1 HCAPLUS

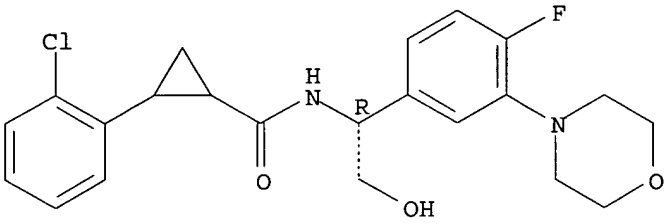
CN Cyclopropanecarboxamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



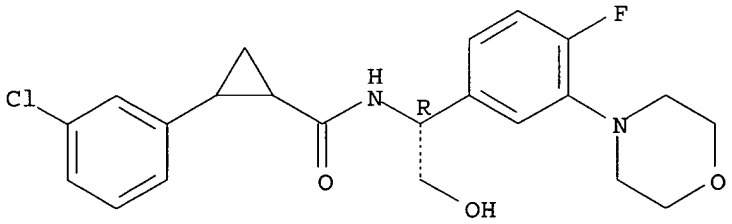
RN 701913-78-2 HCAPLUS
CN Cyclopropanecarboxamide, 2-(2-chlorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



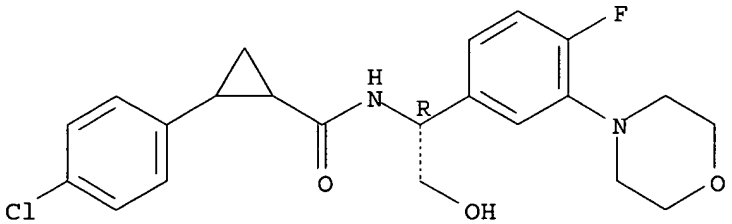
RN 701913-79-3 HCAPLUS
CN Cyclopropanecarboxamide, 2-(3-chlorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 701913-80-6 HCAPLUS
CN Cyclopropanecarboxamide, 2-(4-chlorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]- (9CI) (CA INDEX NAME)

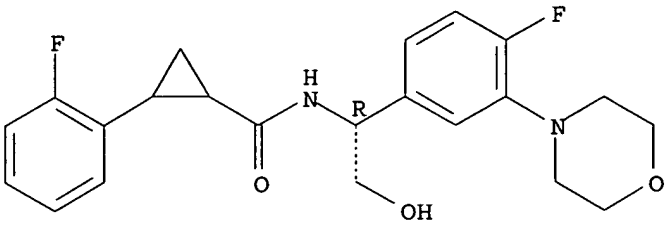
Absolute stereochemistry.



RN 701913-81-7 HCAPLUS

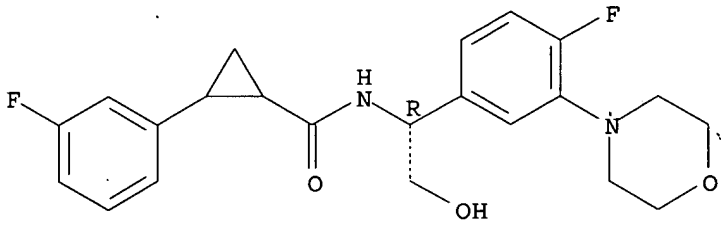
CN Cyclopropanecarboxamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 701913-82-8 HCAPLUS
CN Cyclopropanecarboxamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-2-(3-fluorophenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



544/169
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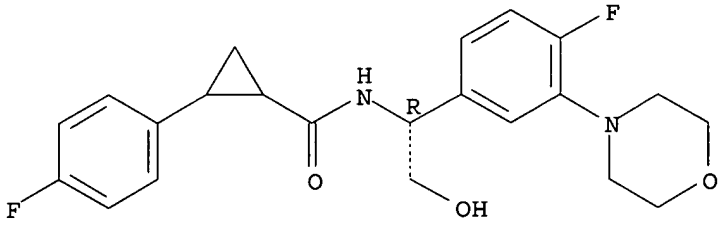
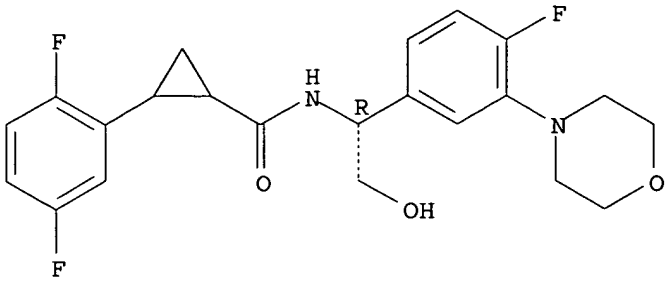
RN 701913-83-9 HCAPLUS
CN Cyclopropanecarboxamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-2-(4-fluorophenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 701913-84-0 HCAPLUS
CN Cyclopropanecarboxamide, 2-(2,5-difluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:467693 HCAPLUS
DOCUMENT NUMBER: 141:38621
TITLE: Preparation of N-(1-aryl-2-hydroxyethyl) amides as potassium channel openers
INVENTOR(S): Wu, Yong-Jin; Sun, Li-Qiang; He, Huan; L'Heureux, Alexandre
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047743	A2	20040610	WO 2003-US37348	20031121
WO 2004047743	A3	20040729		
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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PRIORITY APPLN. INFO.: US 2002-428338P P 20021122
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OTHER SOURCE(S): MARPAT 141:38621
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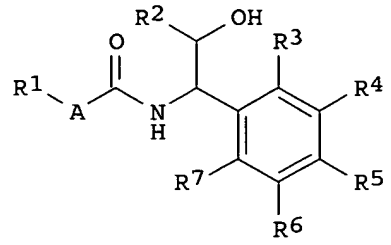

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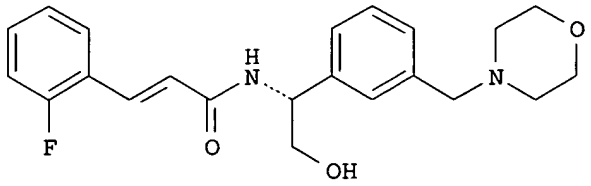

II

AB The title compds. [I; R1 = pyridinyl, 3-quinolinyl, 2-thienyl, furanyl, cycloalkyl, Ph; A = CH:CH, (CH2)n; R2 = H, hydroxymethyl; n = 0-2; R4 = dialkylamino, OCF3, morpholin-4-yl, etc.; R5 = H, F; or R4 and R5 taken together = (un)substituted CH:CHCH:CH; R3, R6, R7 = H, F] which are openers or activators of KCNQ potassium channels (biol. data given), were prepared Thus, amidation of (R)-2-amino-2-[3-(morpholin-4-ylmethyl)phenyl]ethanol hydrochloride (preparation given) with 2-fluorocinnamic acid afforded (R)-II. The present invention also provides pharmaceutical compns. comprising compds. I and the method of treatment of disorders sensitive to KCNQ potassium channel opening activity such as migraine or a migraine attack, bipolar disorders, epilepsy, acute and chronic pain and anxiety.

IT **701942-88-3P 701942-89-4P 701942-90-7P**
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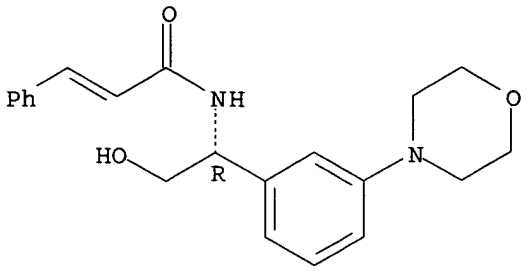
701943-92-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-(1-aryl-2-hydroxyethyl) amides as potassium channel openers)

RN 701942-88-3 HCAPLUS

CN 2-Propenamide, N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 701942-89-4 HCAPLUS
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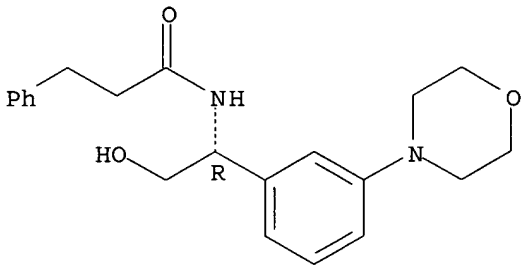
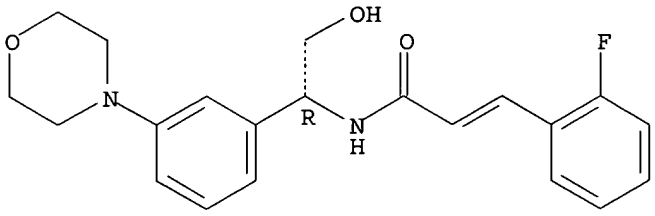
Absolute stereochemistry.



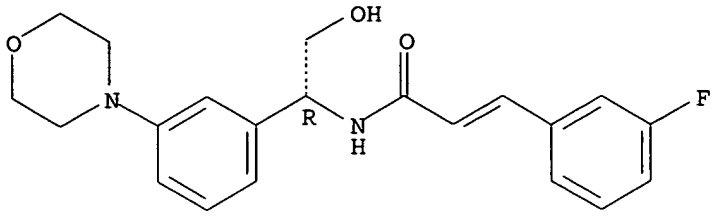
RN 701942-90-7 HCAPLUS
CN 2-Propenamide, 3-(2-fluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



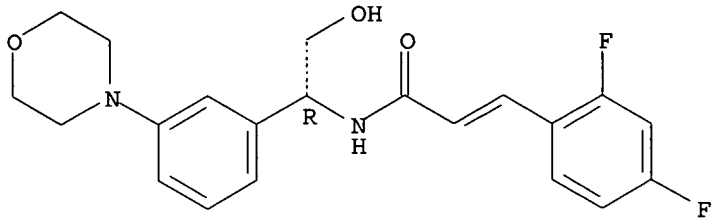
RN 701942-91-8 HCAPLUS
CN 2-Propenamide, 3-(3-fluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



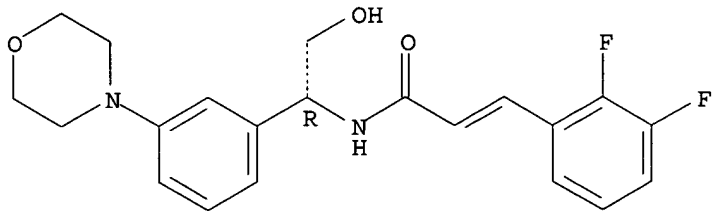
RN 701942-92-9 HCAPLUS
CN 2-Propenamide, 3-(2,4-difluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 701942-93-0 HCAPLUS
CN 2-Propenamide, 3-(2,3-difluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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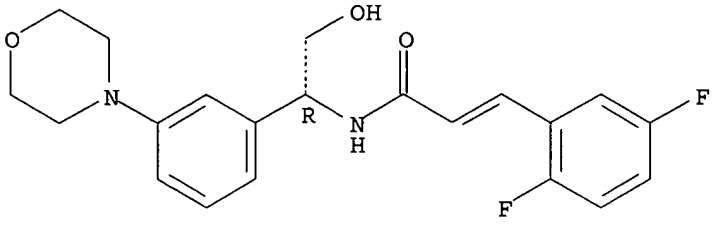
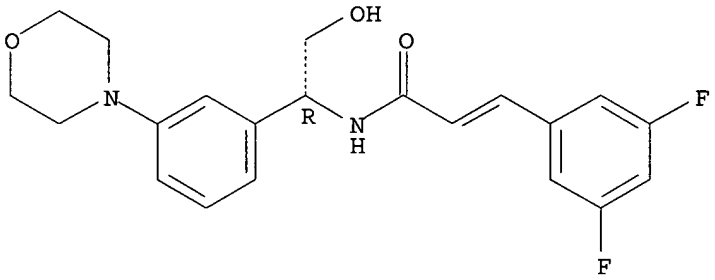
CN 2-Propenamide, 3-(2,5-difluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 701942-95-2 HCAPLUS
CN 2-Propenamide, 3-(3,5-difluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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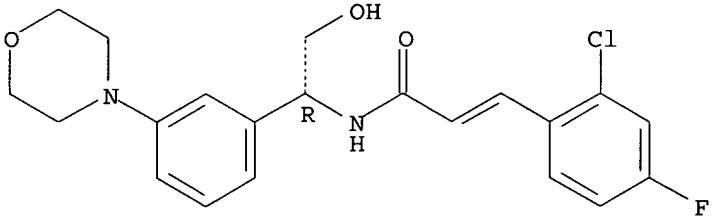
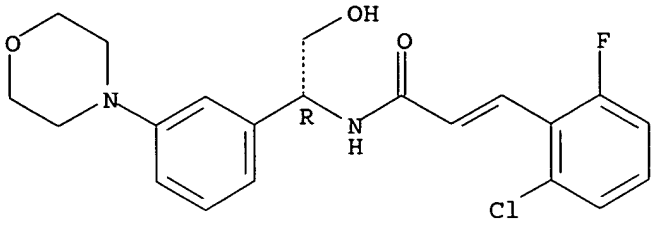
CN 2-Propenamide, 3-(2-chloro-4-fluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



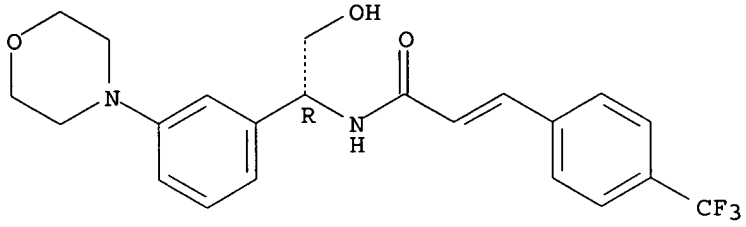
RN 701942-97-4 HCAPLUS
CN 2-Propenamide, 3-(2-chloro-6-fluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



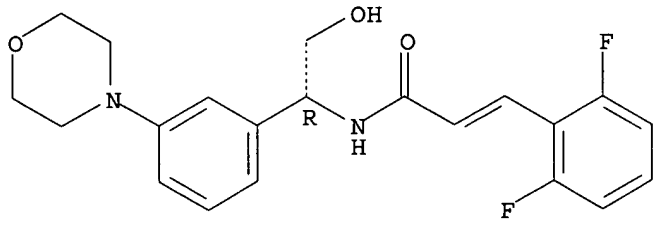
RN 701942-98-5 HCAPLUS
CN 2-Propenamide, N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



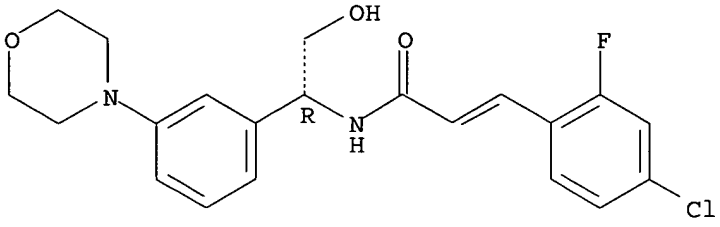
RN 701942-99-6 HCAPLUS
CN 2-Propenamide, 3-(2,6-difluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



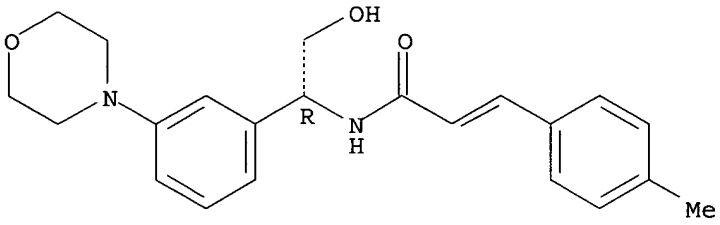
RN 701943-00-2 HCAPLUS
CN 2-Propenamide, 3-(4-chloro-2-fluorophenyl)-N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



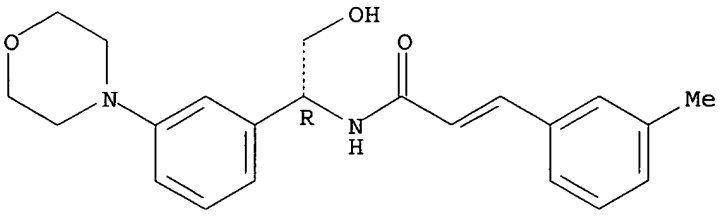
RN 701943-01-3 HCAPLUS
CN 2-Propenamide, N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]-3-(4-methylphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



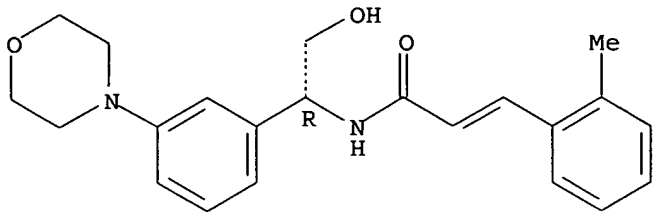
RN 701943-02-4 HCAPLUS
CN 2-Propenamide, N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]-3-(3-methylphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



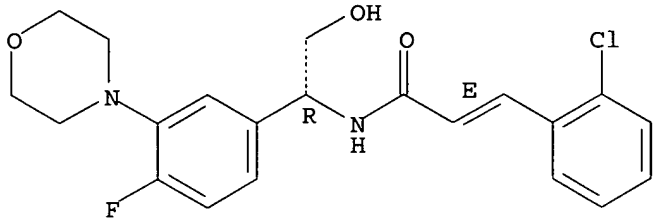
RN 701943-03-5 HCAPLUS
CN 2-Propenamide, N-[(1R)-2-hydroxy-1-[3-(4-morpholinyl)phenyl]ethyl]-3-(2-methylphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



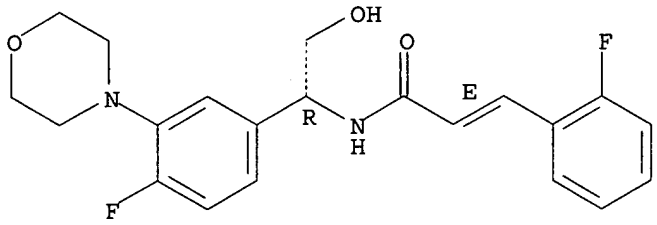
RN 701943-04-6 HCAPLUS
CN 2-Propenamide, 3-(2-chlorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



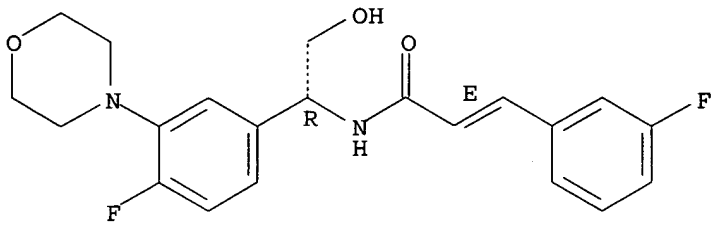
RN 701943-05-7 HCAPLUS
CN 2-Propenamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-3-(2-fluorophenyl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



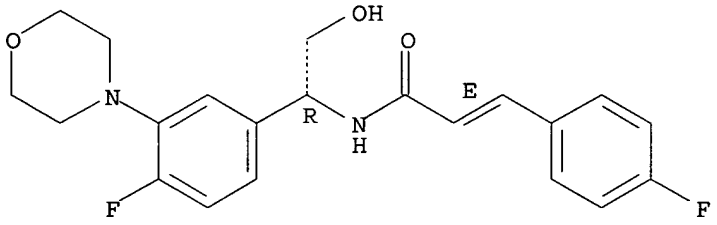
RN 701943-06-8 HCAPLUS
CN 2-Propenamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-3-(3-fluorophenyl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



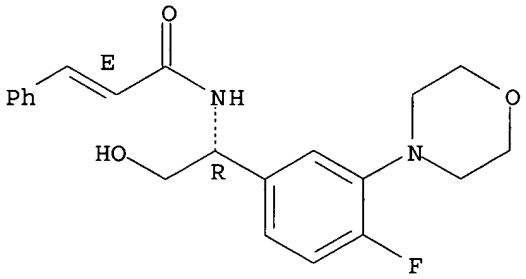
RN 701943-07-9 HCAPLUS
CN 2-Propenamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-3-(4-fluorophenyl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



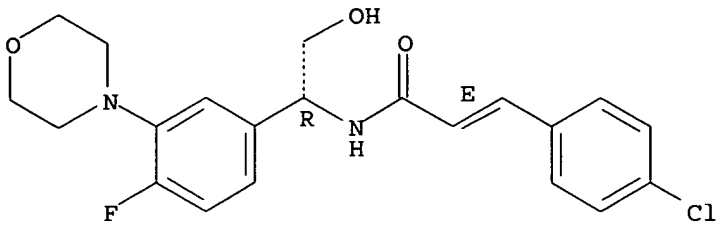
RN 701943-08-0 HCAPLUS
CN 2-Propenamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-3-phenyl-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



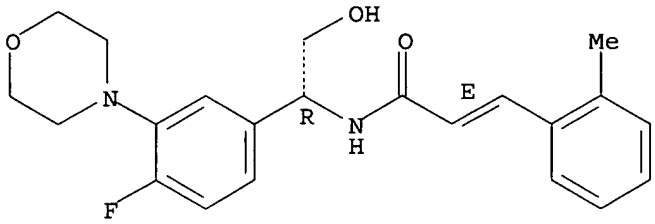
RN 701943-09-1 HCAPLUS
CN 2-Propenamide, 3-(4-chlorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



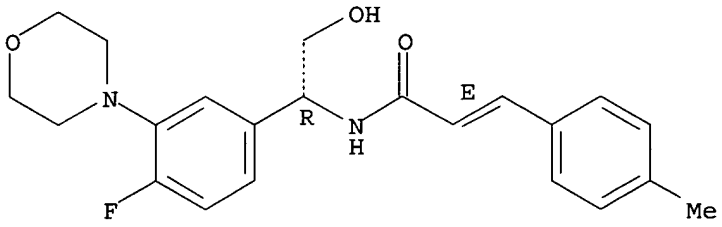
RN 701943-10-4 HCAPLUS
CN 2-Propenamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-3-(2-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



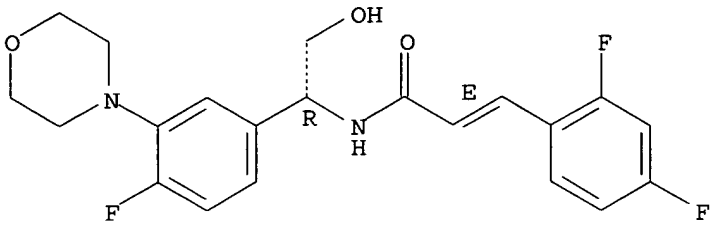
RN 701943-11-5 HCAPLUS
CN 2-Propenamide, N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-3-(4-methylphenyl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



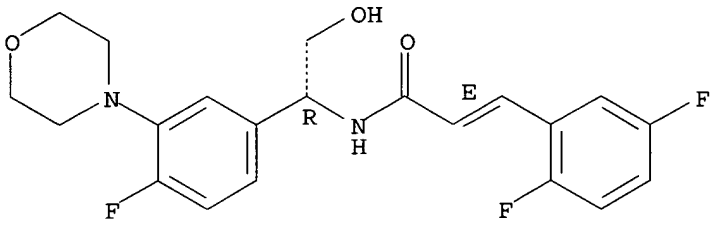
RN 701943-12-6 HCAPLUS
CN 2-Propenamide, 3-(2,4-difluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



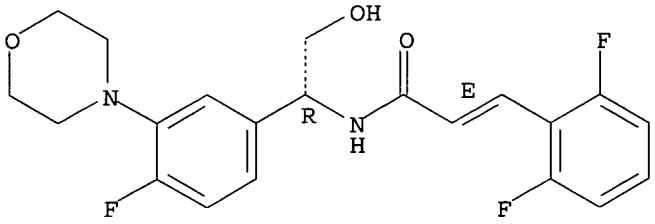
RN 701943-13-7 HCAPLUS
CN 2-Propenamide, 3-(2,5-difluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



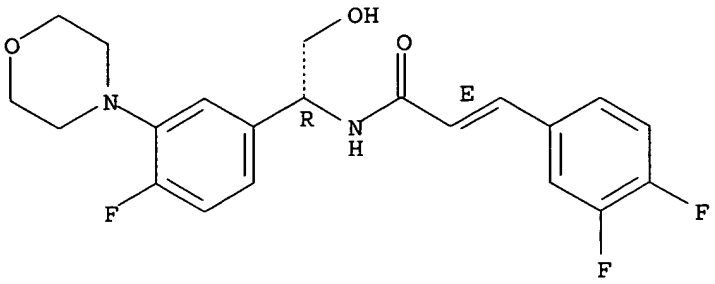
RN 701943-14-8 HCAPLUS
CN 2-Propenamide, 3-(2,6-difluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



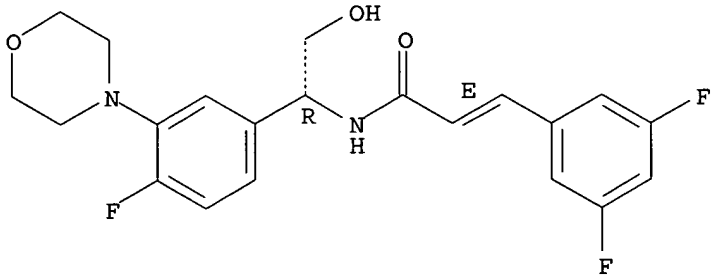
RN 701943-15-9 HCAPLUS
CN 2-Propenamide, 3-(3,4-difluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



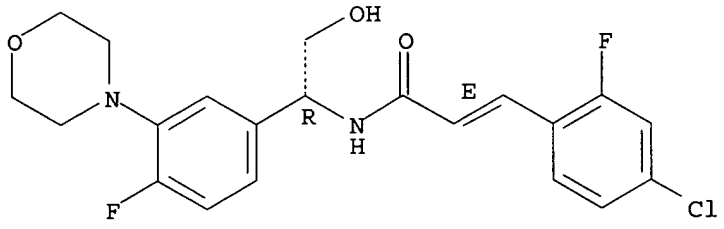
RN 701943-16-0 HCAPLUS
CN 2-Propenamide, 3-(3,5-difluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



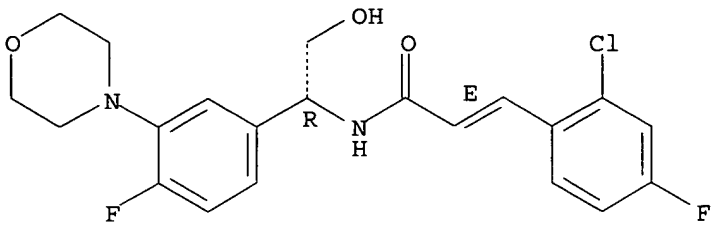
RN 701943-17-1 HCAPLUS
CN 2-Propenamide, 3-(4-chloro-2-fluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



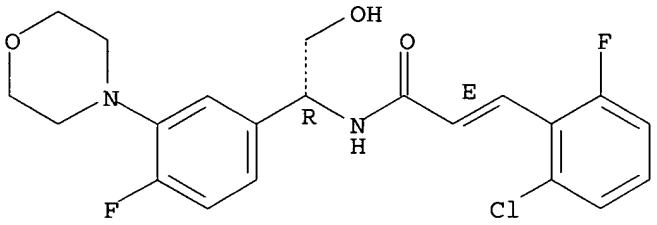
RN 701943-18-2 HCAPLUS
CN 2-Propenamide, 3-(2-chloro-4-fluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



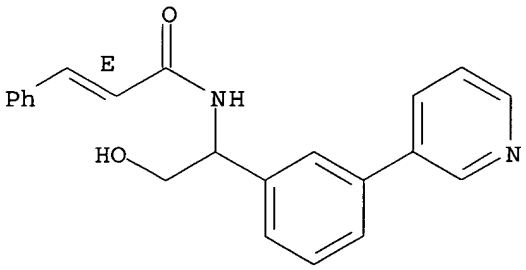
RN 701943-19-3 HCAPLUS
CN 2-Propenamide, 3-(2-chloro-6-fluorophenyl)-N-[(1R)-1-[4-fluoro-3-(4-morpholinyl)phenyl]-2-hydroxyethyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

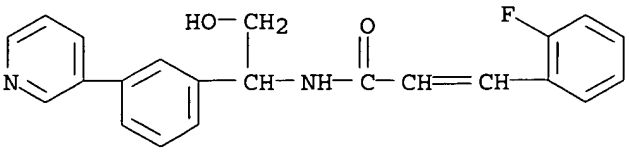


RN 701943-91-1 HCAPLUS
CN 2-Propenamide, N-[2-hydroxy-1-[3-(3-pyridinyl)phenyl]ethyl]-3-phenyl-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 701943-92-2 HCAPLUS
CN 2-Propenamide, 3-(2-fluorophenyl)-N-[2-hydroxy-1-[3-(3-pyridinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

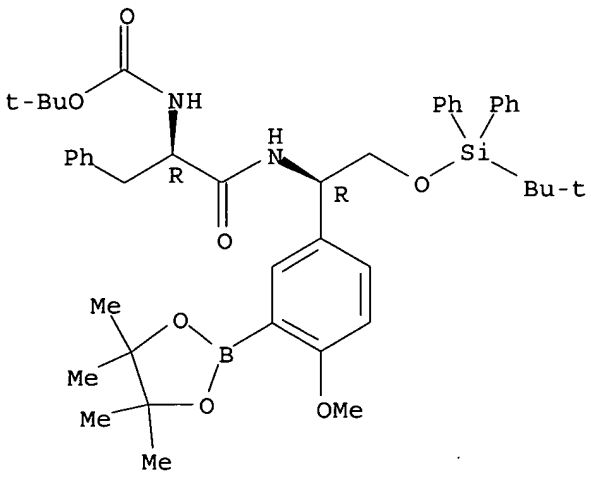
ACCESSION NUMBER: 1999:629455 HCAPLUS
DOCUMENT NUMBER: 131:351666
TITLE: Two Syntheses of the 16- and 17-Membered DEF Ring Systems of Chloropeptin and Complestatin
AUTHOR(S): Elder, Amy M.; Rich, Daniel H.
CORPORATE SOURCE: Department of Chemistry and School of Pharmacy, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Organic Letters (1999), 1(9), 1443-1446
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:351666

AB Two syntheses of a model system of the DEF ring system of complestatin and chloropeptin are described. The key step in both of these syntheses involves the formation of the biaryl linkage using a palladium-catalyzed Suzuki cross-coupling reaction and a catalytic enantioselective ene reaction to form the 6-bromo-D-tryptophan. Addnl., ring contraction of the 17-membered DEF ring system of complestatin generates the 16-membered DEF ring system of chloropeptin in a biomimetic fashion.

IT **250608-85-6P 250608-86-7P 250608-87-8P**
250608-88-9P 250608-89-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of in the synthesis of the 16- and 17-membered DEF ring systems of chloropeptin and complestatin)

RN 250608-85-6 HCAPLUS
CN 8-Oxa-2,5-diaza-9-silaundecanoic acid, 6-[4-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-10,10-dimethyl-4-oxo-9,9-diphenyl-3-(phenylmethyl)-, 1,1-dimethylethyl ester, (3R,6R)- (9CI) (CA INDEX NAME)

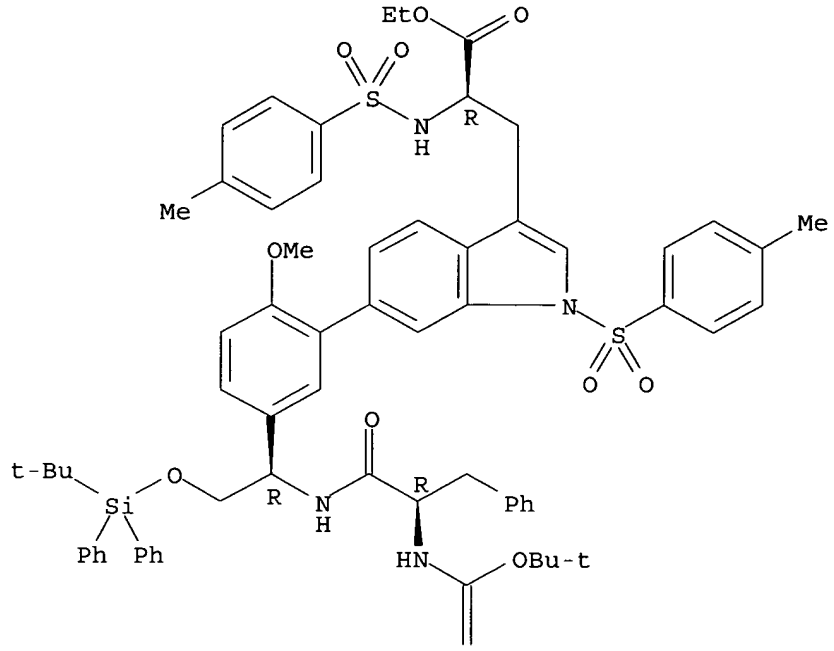
Absolute stereochemistry.



RN 250608-86-7 HCAPLUS
CN D-Tryptophan, 6-[5-[(1R)-1-[[(2R)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-3-phenylpropyl]amino]-2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]ethyl]-2-methoxyphenyl]-N,1-bis[(4-methylphenyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

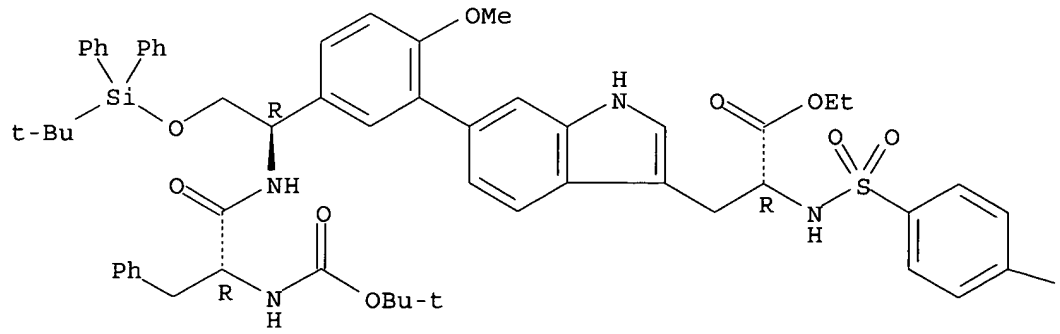


PAGE 2-A

RN 250608-87-8 HCAPLUS
CN D-Tryptophan, 6-[5-[(1R)-1-[[(2R)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-3-phenylpropyl]amino]-2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]ethyl]-2-methoxyphenyl]-N-[(4-methylphenyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



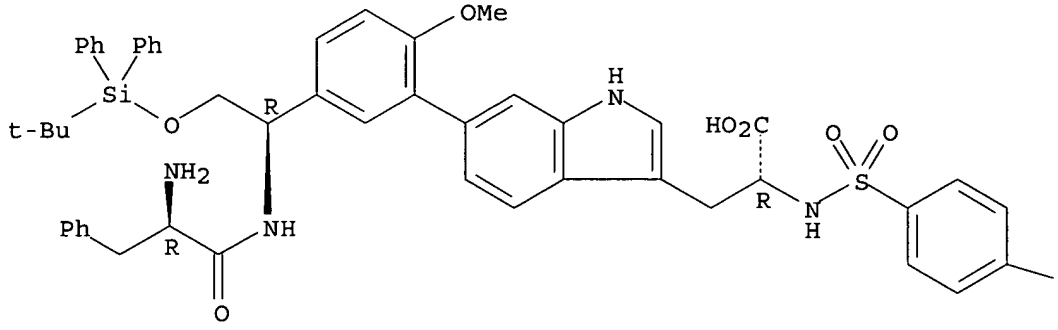
PAGE 1-B

Me

RN 250608-88-9 HCAPLUS
CN D-Tryptophan, 6-[5-[(1R)-1-[[(2R)-2-amino-1-oxo-3-phenylpropyl]amino]-2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]ethyl]-2-methoxyphenyl]-N-[(4-methylphenyl)sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



● HCl

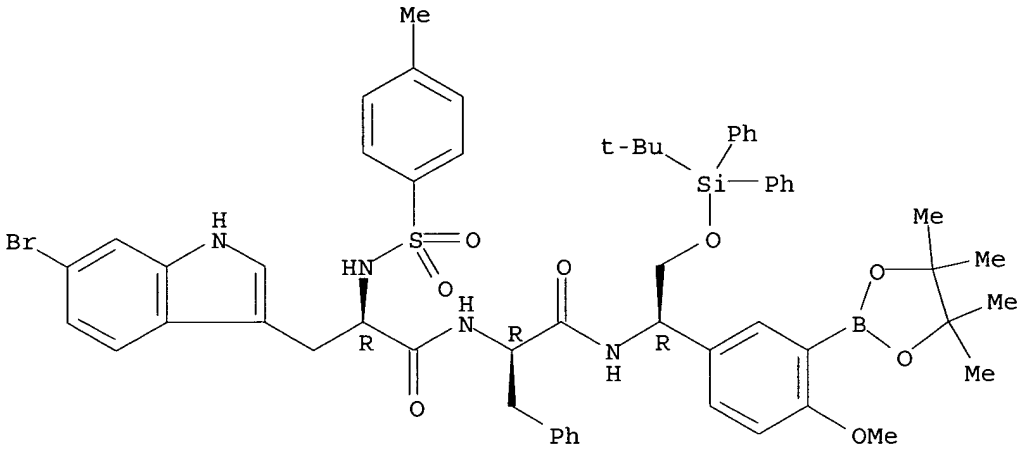
PAGE 1-B

Me

RN 250608-89-0 HCAPLUS
CN D-Phenylalaninamide, 6-bromo-N-[(4-methylphenyl)sulfonyl]-D-tryptophyl-N-

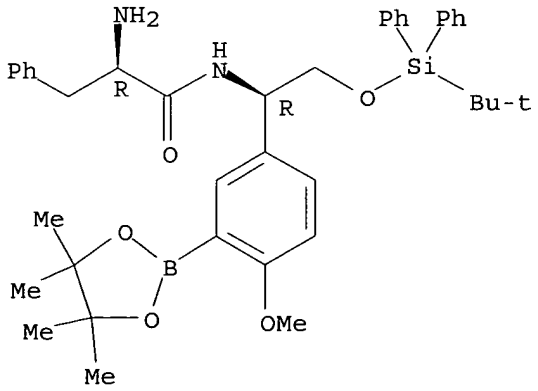
[(1R)-2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-[4-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **250608-77-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of in the synthesis of the 16- and 17-membered DEF ring systems of chloropeptin and complestatin)
RN 250608-77-6 HCAPLUS
CN Benzenepropanamide, α-amino-N-[(1R)-2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-[4-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethyl]-, monohydrochloride, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:238389 HCAPLUS

DOCUMENT NUMBER: 126:287587
TITLE: Probing the Environment of Tubulin-Bound Paclitaxel Using Fluorescent Paclitaxel Analogs
AUTHOR(S): Sengupta, Suparna; Boge, Thomas C.; Liu, Yanbin; Hepperle, Michael; Georg, Gunda I.; Himes, Richard H.
CORPORATE SOURCE: Departments of Biochemistry and Medicinal Chemistry, University of Kansas, Lawrence, KS, 66045, USA
SOURCE: Biochemistry (1997), 36(17), 5179-5184
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

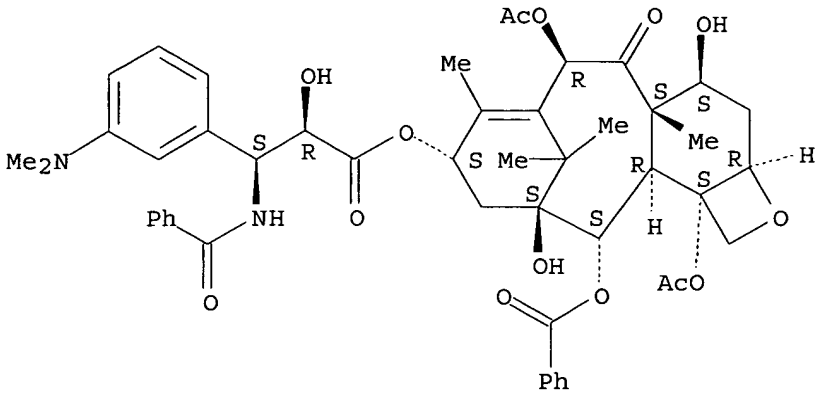
AB To determine the environment of different positions in the paclitaxel mol. when bound to tubulin, we have synthesized six fluorescent analogs in which a (dimethylamino)benzoyl group has been introduced into the 7- and 10-positions, and the benzoyl groups at the 2- and N- as well as the 3'-Ph ring have been modified with dimethylamino functions. In a tubulin assembly assay, the N-m- and N-p-(dimethylamino)benzoyl derivs. had activities comparable to the activity of paclitaxel. The 2-, 3'-, and 10-analogs had slightly reduced activity, and the 7-derivative was about 5% as active as paclitaxel. On the basis of the results of studies of the effect of solvents on the fluorescence emission spectra, it is proposed that the unbound analogs form hydrogen bonds with protic solvents. But the 7- and 10-substituted analogs appear to be more affected by protic solvents than the other analogs. Previously, we studied the binding of the N-meta derivative to tubulin and microtubules [Sengupta, S., et al. (1995) Biochem. 34, 11889-11894]. In this study, we extended the studies to include the 2-, 7-, and 10-derivs. Similar to the N-substituted analog, binding of the 2-derivative to tubulin was accompanied by a large blue shift, whereas a very small shift occurred when the 7- and 10-substituted derivs. bound. The 2- and N-substituted analogs bind to microtubules with an increase in fluorescence intensity over that which was observed with tubulin, whereas binding of the 7- and 10-substituted analogs was accompanied by a large quenching in fluorescence. This quenching may be due to the presence of charged residues in the protein near the 7- and 10-(dimethylamino)benzoyl groups or to π stacking of the groups with an aromatic side chain. The presence of paclitaxel with microtubules prevented the fluorescence increase of the 2- and N-derivs. and quenching of the 7- and 10-derivs. The difference in behavior of the fluorescent analogs upon binding to polymerized tubulin, coupled with the solvent studies on the free drugs, suggests that the 2- and N-benzoyl groups of paclitaxel bind in a hydrophobic pocket of tubulin but could participate in hydrogen bonding, and the 7- and 10-positions are in a more hydrophilic environment.

IT **160313-76-8**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(tubulin binding by fluorescent paclitaxel analogs)

RN 160313-76-8 HCAPLUS

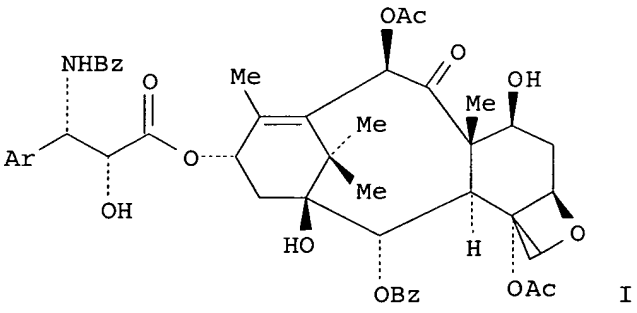
CN Benzenepropanoic acid, β-(benzoylamino)-3-(dimethylamino)-α-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(αR*,βS*),11α,12α,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

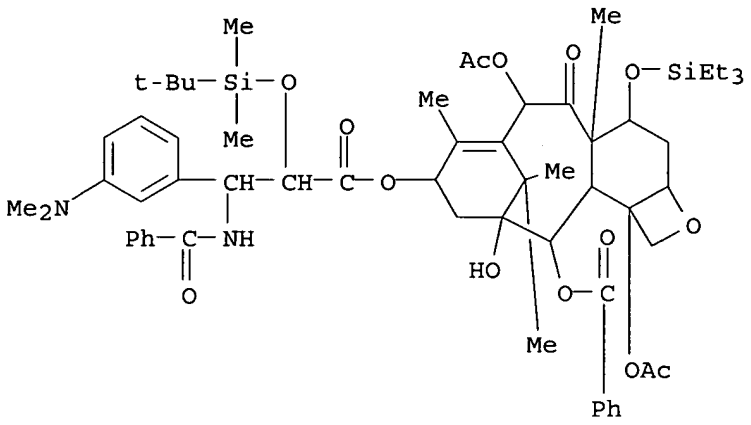
L8 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:120883 HCAPLUS
DOCUMENT NUMBER: 122:81681
TITLE: Synthesis and biology of substituted 3'-phenyl taxol analogs
AUTHOR(S): Georg, Gunda I.; Cheruvallath, Zacharia S.; Harriman, Geraldine C. B.; Hepperle, Michael; Park, Haeil; Himes, Richard H.
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Kansas, Lawrence, KS, 66045, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(19), 2331-6
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:81681
GI



I

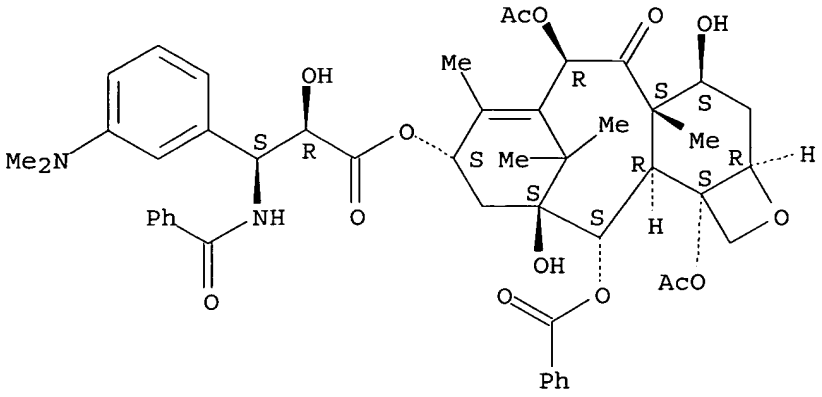
AB A series of substituted 3'-Ph taxol analogs I (Ar = 4-ClC6H4, 4-MeC6H4, 4-MeOC6H4, 2-Me6H4, etc.), directed by the Topliss Operational Scheme, were synthesized and evaluated for their biol. activity. The novel analogs were prepared from baccatin III and N-acyl β-lactams. Evaluation in the microtubule assembly assay and for cytotoxicity against B16 melanoma cells illustrated a modest influence of aromatic substitution on bioactivity.

IT **160314-00-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of taxol analogs, their tubulin assembly promotion and antitumor activity)
RN 160314-00-1 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-3-(dimethylamino)-α-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-[(triethylsilyl)oxy]-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(αR*,βS*),11α,12α,12aα,12bα]]- (9CI) (CA INDEX NAME)



IT **160313-76-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, tubulin assembly promotion, and antitumor activity)
RN 160313-76-8 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-3-(dimethylamino)-α-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, [2aR-[2aα,4β,4aβ,6β,9α(αR*,βS*),11α,12α,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:68704 HCAPLUS
DOCUMENT NUMBER: 96:68704
TITLE: Cephalosporin derivatives and pharmaceutical compositions containing them
INVENTOR(S): Wehrli, Hansuli; Kocsis, Karoly; Scartazzini, Riccardo
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 177 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 31794	A2	19810708	EP 1980-810386	19801215
EP 31794	A3	19820203		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4464366	A	19840807	US 1980-214155	19801208
ES 497849	A1	19811116	ES 1980-497849	19801217
DK 8005408	A	19810620	DK 1980-5408	19801218
AU 8065518	A1	19810625	AU 1980-65518	19801218
ZA 8007914	A	19820127	ZA 1980-7914	19801218
JP 56103186	A2	19810818	JP 1980-181821	19801219
PRIORITY APPLN. INFO.:			CH 1979-11283 A	19791219

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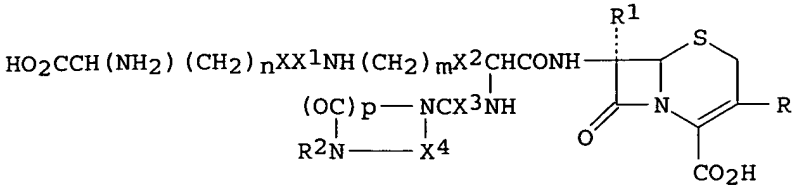

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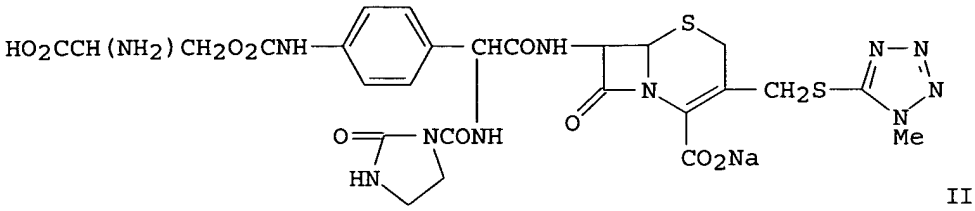


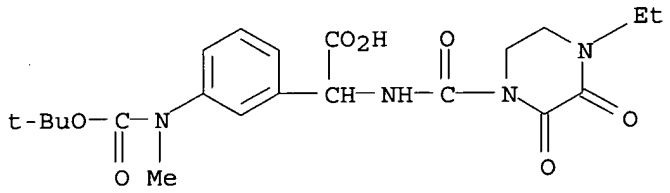
II

AB Cephalosporins I [m = 0, 1; n = 1-4; p = 1, 2; X = O, S, NH, bond; X1 = CO, CONHSO2, SO2NHCO; X2 = (un)substituted phenylene, thienylene, furylene; X3 = O, S; X4 = alkylene; R = H, alkyl, alkoxy, halo, esterified or etherified CH2OH, CH2SH, ammoniummethyl; R1 = H, OMe; R2 = H, (un)substituted alkyl, cycloalkyl, acyl] were prepared as bactericides (no data). Thus II was obtained from the aminocephem by a 2-step acylation and deblocking.

IT **79537-77-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of aminocephems by)

RN 79537-77-2 HCAPLUS

CN Benzeneacetic acid, 3-[[(1,1-dimethylethoxy)carbonyl]methylamino]-α-[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

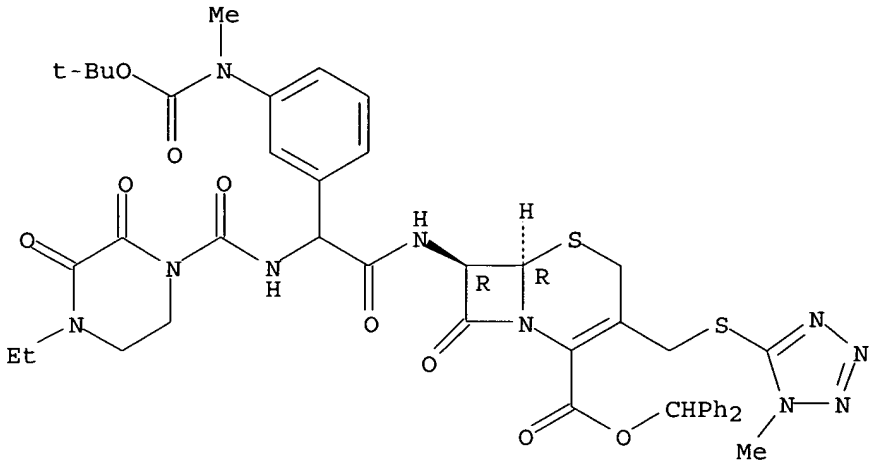


IT **79537-79-4P 79553-65-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)

RN 79537-79-4 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[[3-[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl][[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]acetyl]amino]-3-[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-, diphenylmethyl ester, [6R-(6α,7β)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 79553-65-4 HCAPLUS
CN D-Serine, N-[(1,1-dimethylethoxy)carbonyl]-, diphenylmethyl ester, [3-[2-[[2-[(diphenylmethoxy)carbonyl]-3-[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl]amino]-1-[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]-2-oxoethyl]phenyl]methylcarbamate (ester), [6R-(6α,7β)]- (9CI) (CA INDEX NAME)

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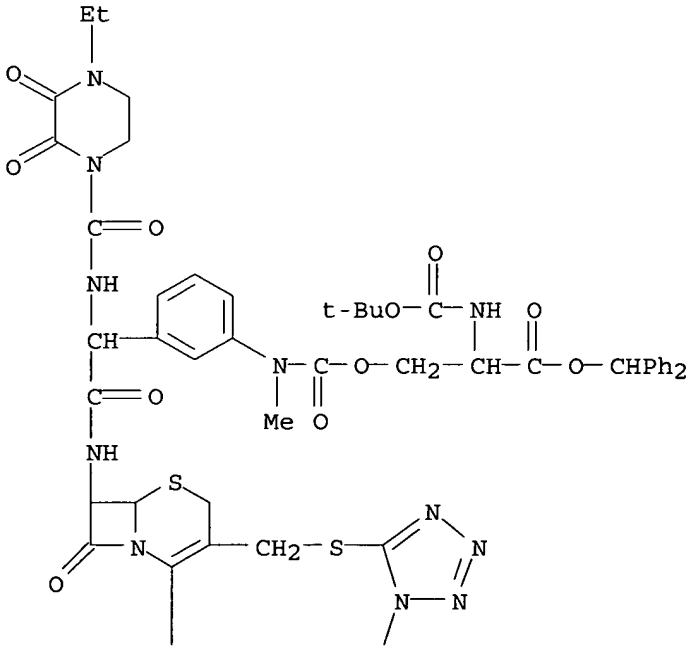
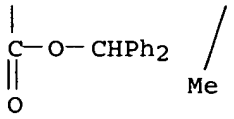


PAGE 2-A



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